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Original Article

Development of a Paediatric-Friendly Pullulan-Based Mouth Dissolving Film of Ferrous Bisglycinate Using Factorial Design and Electronic Tongue-Assisted Taste Evaluation

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ABSTRACT

Background: The primary objective of this study was to develop, optimize and evaluate a paediatric-friendly, pullulan-based Mouth Dissolving Film (MDF) of Ferrous Bisglycinate as a novel iron delivery system. The work aimed at improving bioavailability, minimizing gastrointestinal side effects, and enhancing patient compliance in the management of iron deficiency anaemia, which is the one of the symptoms of malnutrition in children. Ferrous Bisglycinate has been specifically selected as the iron source due to its chelated structure with two glycine molecules, which provides superior absorption, reduced interaction with dietary inhibitors, and lower gastrointestinal irritation compared to conventional ferrous and ferric salts. **Materials and Methods:** MDF was formulated using polymers [Hydroxy Propyl Methyl Cellulose (HPMC) E15, Lycoat RS® 720, and Pullulan] and plasticizers [Poly ethylene Glycol (PEG) 400, Glycerol] by the solvent casting method. The formulated film was evaluated for various parameters like Disintegration Time (D.T), thickness, tensile strength, Young's modulus, % elongation, % assay and pH. Further, Pullulan with PEG 400 was optimized using a 3^2-factorial design. Optimized formulation was further evaluated for *in vitro* dissolution study, stability studies, FTIR studies, taste profiling using electronic tongue (e-tongue), taste evaluation on human volunteers and microbial contamination test for non-sterile products. **Results and Discussion:** MDF with Pullulan (6%w/v) and PEG 400 (3.78%w/v) showed required characteristics including acceptable organoleptic properties confirmed by the e tongue and human volunteers study, stability over a six-month storage period, and compliance with microbial contamination limits. **Conclusion:** Developing MDF for Ferrous Bisglycinate holds the potential to establish a Platform technology for other micronutrients.

Keywords: Electronic Tongue, Ferrous Bisglycinate, Malnutrition, Micronutrients, Mouth-dissolving film.

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INTRODUCTION

A deficiency or imbalance in nutrient intake is termed as malnutrition. It is estimated that approximately 45% of deaths among children under five globally are associated with malnutrition, including its effects on immune function, growth and development (*World Health Organization,Malnutrition*, 2025). Among these deaths, about 12% are attributable to micronutrient deficiencies-particularly deficits of zinc, iron, iodine, and Vitamin A-that significantly increase vulnerability to infectious disease and developmental impairments (Ahmed *et al.*, 2012). A common clinical manifestation of micronutrient deficiency is fatigue, especially persistent tiredness, which is a hallmark of Iron-Deficiency Anaemia (IDA). The World Health Organization (WHO) considers anaemia a serious global public health issue, with the most affected groups being young children (6-59 months), adolescent girls and women of reproductive age, as well as pregnant and postpartum women. According to WHO estimates, about 40% of children aged 6-59 months, around 37-42% of pregnant women, and approximately 30% of non-pregnant women aged 15-49 years are anaemic globally. Of those cases, a substantial proportion is due to iron deficiency (World Health Organization, Anaemia, *2025*). Iron deficiency anaemia can be treated via oral or intravenous routes. Oral iron therapy commonly uses various Ferrous (Fe^{2+}) and Ferric (Fe^{3+}) salts. Absorption of ferrous salt is much higher than that of the ferric salts (Brise and Hallberg, 1962; Santiago, 2012). Different salts of ferrous and ferric are approved by the Food Safety

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Standard Authority of India (FSSAI). (Authority and Delhi, 2018). Among ferrous salts, ferrous sulphate, ferrous fumarate, and ferrous gluconate are widely used, owing to their relatively good elemental iron content and affordability. However, conventional oral iron treatment often has low fractional iron absorption: only about 10-20% of the administered oral dose is absorbed, with the remainder remaining in the gastrointestinal tract. The unabsorbed iron tends to cause gastrointestinal side effects (nausea, constipation, abdominal discomfort, diarrhoea), which in turn reduce patient adherence to therapy (Pantopoulos, 2024). There are many oral formulations available for the management of iron deficiency anaemia like tablets, capsules, syrups etc. As per our knowledge, these conventional dosage forms are available in the market, but a cost-effective and patient-friendly formulation containing iron is not available. This provokes a need for novel dosage forms like Mouth Dissolving Film (MDF) containing the iron to improve the bioavailability with better patient compliance. In this context, ferrous bisglycinate has emerged as a promising alternative. It is an iron chelated with two molecules of glycine, which appears to have better absorption, less interaction with dietary inhibitors of iron absorption, and fewer gastrointestinal side effects compared to many conventional ferrous and ferric salts (Yu *et al*., 2019).

MDF possesses several advantages over the conventional dosage form in terms of pleasant taste, no need of water for swallowing, no choking issues, dose accuracy and greater stability as compared to liquid dosage form, rapid disintegration and thereby increase in dissolution due to large surface area, ease in manufacturing, handling and storage (Jain *et al*., 2023 and Palezi *et al*., 2023). However, it gives difficulty in incorporating the large dose. Moreover, it requires low molecular weight and good solubility of the drug in water or saliva, and requires special storage and packaging (Dixit and Puthli, 2009; Karki *et al*., 2016). For children aged 2-5 years and 5-12 years, the recommended daily elemental iron supplementation is approximately 30 mg and 30-60 mg, respectively. Accordingly, the formulated MDF was designed to deliver Ferrous Bisglycinate equivalent to 15mg of elemental Fe^{2+} per unit dose (Chan and Mike, 2014; World Health Organization, 2016).

Human study for taste evaluation

Six human volunteers participated in the study. The study described was approved by the Institutional Ethics Committee (IEC) at Nirma University (IEC/NU/24/IP/01). Written informed consent was obtained from each Participant.

MATERIALS AND METHODS

Materials

Ferrous Bisglycinate, Sucralose, Citric acid, Mixed fruit flavour obtained as a gift sample from Syzer Life Science (Ahmedabad, Gujarat, India), Sweet pearl P 300 DC and Lycoat RS® 720 obtained as gift sample from Roquette Pharma (France), Pullulan purchased from Yarrow Chem Products (Mumbai, India). Glycerol, Polyethylene Glycol (PEG) 400, and trisodium citrate were used laboratory grade. The water used was distilled water. Ossoro Spanish Strawberry and coffee aroma flavour purchased online.

Based on the literature referred for MDF, the general formula for MDF and the objective of selection component of MDF are as follows (Jain *et al*., 2023; Pacheco *et al*., 2021; Salawi, 2022).

Film Formers

Lycoat® RS720 (Hydroxypropyl Pea Starch): Selected for its excellent film-forming and coating properties, making it suitable for use in both pharmaceutical and nutraceutical formulations (Alayoubi *et al*., 2017).

Pullulan: It was chosen because it forms uniform, transparent, and hydrophilic films that disintegrate rapidly due to its high water affinity (Prajapati *et al*., 2018).

Plasticizers

Polyethylene Glycol (PEG 400) and Glycerol: Included to enhance the elasticity and flexibility of the film, preventing brittleness and ensuring smooth handling (Jain *et al*., 2023).

Sweeteners

Sweet Pearl P300DC : Preferred due to its low hygroscopicity and excellent chemical stability, which help to maintain film integrity (Sheet, 2019).

Sucralose: Used as a non-cariogenic sweetener, providing sweetness without promoting dental caries.

Flavoring Agents

Mixed Fruit, Coffee, and Strawberry Flavors: Added to improve taste and acceptability, making the formulation more suitable for paediatric patients.

Saliva-Stimulating Agent

Citric Acid: Incorporated to provide a pleasant sour taste, which helps in stimulating saliva and enhancing palatability (Lambros *et al*., 2022).

pH Adjuster

Trisodium Citrate: Used to maintain the pH of the formulation within the range of 5-7, ensuring stability and patient comfort.

Solvent

Distilled Water: Served as an aqueous vehicle for the preparation of the film, enabling uniform dispersion of all excipients.

Methodology

Method of preparation of MDF prepared from Lycoat RS 720 as film former

The film was prepared using the solvent casting method (Joshi *et al*., 2012; Reuther *et al*., 2025; Senthilkumar and Vijaya, 2015). The composition of the base formulation is presented in Table 1a, while Table 1b lists the variable concentrations of Lycoat RS® 720 and glycerol employed in the optimization study. The total number of individual MDF units (2 × 2 cm each) that could be produced from a single casting plate was calculated by dividing the surface area of the Petri-plate by the area of one unit film; ingredient quantities were scaled accordingly for MDFs prepared from 100 mL of casting solution. Each unit film contained Ferrous Bisglycinate corresponding to 15 mg of elemental Fe^{2+}.

Initially, the polymeric film-forming solution was prepared by dispersing Lycoat RS® 720 in distilled water and stirring at 300 rpm for 15 min at 30°C using a magnetic stirrer with temperature control (Model MS-4, Deepali). Subsequently, Ferrous Bisglycinate, glycerol, sucralose, Sweet Pearl P300 DC, citric acid, trisodium citrate, and mixed fruit flavor were incorporated sequentially under continued stirring at 300 rpm until complete dissolution. The casting solution was allowed to stand undisturbed for approximately 20 hr to eliminate entrapped air bubbles. Aliquots of 10 mL of the degassed solution were then transferred to the specified Petri-plate (diameter 9 cm) using a pipette. Films were dried in a digital hot-air oven (Model 100, EIE Instruments Pvt. Ltd.,) at 60°C for 3 hr. After drying, the films were carefully peeled off, inspected for surface imperfections, wrapped in aluminium foil, placed in zip-lock bags, and stored in a desiccator until further evaluation. The dried films were cut into 2 × 2 cm squares, each containing Ferrous Bisglycinate equivalent to 15 mg of elemental Fe^{2+}

Method of preparation of MDF prepared from Pullulan as film former

A homogeneous polymeric solution was initially prepared by dispersing the Pullulan in distilled water and stirring on a temperature-controlled magnetic stirrer (Model MS-4, Deepali, India) at 300 rpm for 15 min at 30°C (Mishra and Amin *et al*., 2011; Pacheco *et al*., 2021). Subsequently, Ferrous Bisglycinate, PEG 400, sucralose, Sweet Pearl P300 DC, tri-sodium citrate and flavour were incorporated sequentially under continuous stirring at 300 rpm until complete dissolution. The resulting solution was assessed for "Brix value" (using Hamh optics and tools refractometer with Automatic temperature compensation) (*Degrees Brix to Specific Gravity*, 2011; John Anthony Considine, 2023) to ensure consistency of solids content. Aliquots of 10 mL of the casting solution were transferred to plastic Petri-plates (diameter 9 cm) using a pipette and dried in a digital hot-air oven (Model 100, EIE Instruments Pvt. Ltd., India) at 60°C for the specified duration. The dried films were carefully peeled off, inspected visually for surface defects, wrapped in aluminium foil, sealed in zip-lock bags and stored in a desiccator until further evaluation. The films were cut into 2×2 cm squares, each containing Ferrous Bisglycinate equivalent to 15 mg of elemental Fe^{2+}. Batches formulated with pullulan and PEG 400 in varying concentrations are summarised in Table 1c.

Evaluation of MDF

The MDF was evaluated for Disintegration Time (D.T), thickness, tensile strength, Young's modulus, % elongation, % assay and pH. The optimized batch was further assessed for *in vitro* dissolution studies, stability studies, FTIR studies, taste profiling using *e-tongue*, taste evaluation using human volunteers, microbial contamination tests.

Disintegration time (Mishra and Amin *et al*., 2011; Senthilkumar and Vijaya, 2015)**:** D.T. was determined by the modified disintegration method using the Petri-plate method. 10 mL of distilled water was placed into the petri-plate, and then the film (2cmx2cm) was placed onto the stainless-steel wire mesh. The time in seconds required to disintegrate the film was noted as the disintegration time. The test was performed in triplicate

Thickness (Mishra and Amin *et al*., 2011; Senthilkumar and Vijaya, 2015)**:** It is measured by a digital thickness gauge (Mitotoyo Corporation) at five different points, and the result was noted as an average (MD *et al*., 2023).

Mechanical Parameters (Senthilkumar and Vijaya, 2015)**:** Mechanical characteristics of the films-including tensile strength, Young's modulus, and percentage elongation-were assessed using a digital tensile testing apparatus (Model SE-2000, EIE Instruments Pvt. Ltd., Ahmedabad, India). Each film is mounted between the two probes of the instrument. The initial length between the two probes was kept at 2.5 cm, and the breadth of the film was 2 cm. Two probes were allowed to move in opposite directions at a 20 mm/min speed. The peak load (Kg) at which the film broke was measured and the final length between the two probes was also determined.

Tensile strength: It is the maximum stress applied to a point at which the strip specimen breaks.

$$\text{Tensile strength} = \text{Peak Load/Cross-sectional area of film} \quad \text{----------(1)}$$

$$\text{Young's Modulus} = \frac{\text{Peak Load}}{\text{Area} \times \text{strain}} \quad \text{----------(2)}$$

Where, Strain = Final length/Initial Length

% Elongation: It depicts the flexibility of the film.

$$\% \text{ Elongation} = \frac{\text{Final length- initial length}}{\text{initial length}} * 100 \quad \text{----------(3)}$$

% Assay (Uses, 2003)**:** Dissolve about 1 g of dry sample into the mixture of 150 mL of water and 10 mL of sulfuric acid TS. Add 1

drop of ortho-phenanthroline TS. Immediately titrate with 0.1 N ceric sulphate. Identically perform blank determination and do necessary corrections. Each mL 0.1 N ceric sulphate is equivalent to 5.585mg of ferrous ion

pH: The film was moistened with 0.5 mL of distilled water and kept for 30 sec (MD *et al.*, 2023). pH was measured using a calibrated digital pH meter (Analab Scientific Instruments Pvt. Ltd.,)

Dissolution studies (Sunita *et al.*, 2012): The dissolution studies was conducted for an optimized batch utilizing dissolution apparatus USP type II (paddle) (Dissolution tester USP, TDL-08L, Electrolab). A strip (2x2cm^2) containing the iron equivalent to 15mg was taken for the study. 900 mL of distilled water was utilized as a dissolution medium. The paddle was rotated at a speed of 50 rpm, and the temperature of the dissolution bath was 37±0.5°C. 5 mL of Samples were withdrawn at 2, 5, 10, 15, 20, 30, 60 min, with an equal volume of distilled water replaced after each sampling. The iron content in these samples was quantitatively determined using UV spectrophotometer (UV 1800, Shimadzu) at λ_{max} 510 nm. Additionally, dissolution studies were also performed for Ferrous Bisglycinate powder (weight of powder was equivalent 15 mg of Ferrous Bisglycinate) using the same method.

Stability Studies: The optimized MDFs were subjected to stability studies. The films were wrapped in aluminum bag (Smart pack aluminum pouches for food and drugs, Thickness: 60 microns) and kept in zip lock bag containing a silica bag and again that zip lock bag wrapped into aluminum bag and kept at 45°C and 75% RH and 25°C and 40% RH for 6 months in humidity chamber and photo-stability chamber (Thermo lab scientific equipment, Vasai, Maharastra, India) respectively (Diaz *et al.*, 2016; ICH, 2003). The films were evaluated for dissolution studies, mechanical parameters, Disintegration time, and % Moisture content at 0, 3, 6 months and results were compared with a 0-month batch as a reference. To assess changes in dissolution profiles, the dissimilarity factor (f_1) and similarity factor (f_2) were calculated. An f_1 value <50 and an f_2 value between 50 and 100 indicate similarity between two profiles.

Table 1a: General formula for MDF of Ferrous Bisglycinate.

Ingredients	Amount
Ferrous Bisglycinate (%w/v)	12
Film former (%w/v)	-
Plasticizer (% w/v)	-
Sweet pearl P 300 DC (%w/v)	5
Citric acid (%w/v)	0.5
Tri Sodium citrate (%w/v)	1.5
Sucralose (%w/v)	0.35
Mixed fruit Flavor	q.s.
Water (mL)	100

Table 1b: MDF with different concentrations of Lycoat RS® 720 and Glycerol.

Batch No.	Ingredients	Amount (% w/v)	Type of surface
F1	Lycoat RS® 720	10	Glass
	Glycerol	3.78	
F2	Lycoat RS® 720	15	Plastic
	Glycerol	3.78	
F3	Lycoat RS® 720	15	
	Glycerol	5.04	
F4	Lycoat RS® 720	15	
	Glycerol	6.3	
F5	Lycoat RS® 720	12	
	Glycerol	3.78	
F6	Lycoat RS® 720	17	
	Glycerol	3.78	
F7	Lycoat RS® 720	15	Teflon coated
	Glycerol	3.78	
F8	Lycoat RS® 720	17	
	Glycerol	3.78	
F9	Lycoat RS® 720	10	-
	HPMC E15	2	
	Glycerol	3.78	

Table 1 c: Formulation of MDF using Pullulan and PEG 400.

Ingredient	F10	F11	F12	F13	F14	F15	F16	F17	F18
Pullulan (%w/v)	5	5	5	6	7	7	8	8	4
PEG 400(%w/v)	3	4	5	3	3	5	5	4	5
Brix value (%)	20.7	20.8	20.8	21.1	21.8	23	23.8	23.8	22.2
pH of casting solution	3-4								
Drying time	2 hr and 15 min								

Table 1 d: Taste evaluation parameters with scores.

Taste Evaluation/ Score	1	2	3	4	5
Metallic taste	Extreme	High	Acceptable	Slightly metallic	Not at all metallic taste
Sweetness	Not at all sweet	Slightly sweet	Acceptable	High	Extreme
Mouth feel	Very gritty	Gritty	Acceptable	Slightly smooth	smooth
Flavor	Very unpleasant	Unpleasant	Acceptable	Pleasant	Very pleasant
Overall palatability	Worst	Poor	Acceptable	Good	excellent
Bitter aftertaste	Most Bitter	Bitter	Acceptable	Slightly bitter	Not bitter
Disintegration time	Less than 30 sec				

FTIR Studies: FTIR studies were conducted for the optimized formulation (F22 batch) and freshly prepared powder mixture using instrument FTIR 6100 (Jasco, Japan) (Yunarti *et al*., 2018).

Taste profiling using electronic tongue (e-tongue)

(Gupta *et al*., 2009; Kumar *et al*., 2021; Nam *et al*., 2023)**:** Taste profiling of the optimized MDF batch was performed using an e-tongue (Astree, Ref AST-059). The system operates by the determination of potential differences between individual sensors and a reference electrode (Ag/AgCl). The device is equipped with seven sensors (AHS, PKS, CTS, NMS, CPS, ANS, and SCS), a reference electrode, and a stirrer. Among them, AHS, CTS, and NMS are selective for sourness, saltiness, and umami, respectively, while PKS, CPS, ANS, and SCS serve as general-purpose sensors. Each sensor membrane exhibits high sensitivity toward ionic and neutral analytes. Responses are generated as potential differences relative to the reference electrode (Wang *et al*., 2021). The sensor array was immersed in 25 mL of sample solutions for 120 sec with 250 rpm stirring, with Milli-Q water rinsing between runs to prevent cross-contamination. MDF was analysed against pure Ferrous Bisglycinate powder to assess whether the taste profile was significantly distinct or not. Both samples were individually dissolved in Milli-Q water, filtered (What man filter), and subjected to e-tongue analysis. Five replicates were prepared, with the initial two and final one excluded to minimize preconditioning and saturation effects. Sensor signals (mV) were processed in AlphaSoft software using multivariate analysis. The drug and MDF were interpreted for Principle component analysis, discrimination index, sensor response data, and bitterness evaluation. Principal Component Analysis (PCA) and discrimination index was employed to determine differences between the pure Ferrous Bislycinate powder and MDF overall taste profiles. PCA transforms multiple correlated sensor outputs into orthogonal principal components; PC1 and PC2 were used to explain sample variance, with PC1+PC2>80% considered representative of most information. Sensor outputs were recorded on a 0-12 scale for all seven sensors. Distinct response for sensors of Ferrous Bisglycinate powder and MDF indicated difference in taste profile. Bitterness evaluation was additionally benchmarked using quinine sulphate as a reference standard**.**

Taste evaluation using Human volunteers

Palatability of the optimized MDF was assessed on six healthy adult volunteers, comprising 3 men (age 35, 42, 44 years) and 3 women (age 35, 42, 43 years). The healthy volunteers were selected randomly. Before each administration, the volunteers were instructed to rinse their mouth with 100 mL of distilled water. The MDF was then placed on the tongue for 30 sec and not allowed to be swallowed. The volunteers were instructed to move the MDF between the tongue and the upper jaw. Any residue from the dosage form was instructed to be expelled, and the mouth was rinsed with distilled water. The taste experienced by each volunteer was recorded and coded using different numbers for each parameter, which is depicted in Table 1d. The average of the taste score of each taste evaluation was considered.

In the present study, it will be ideal to have children, as the proposed formulation is for children. However, it was observed that children's cognitive skills vary. Further, the parent or

guardian's concern is also essential. Thus, in the present study, six human volunteers were taken rather than children. However, children who match with requirements will be explored in future taste evaluation studies (Mathur and Swaminathan, 2018).

Microbial contamination testing

MDF was evaluated for the microbial contamination test for non-sterile products in accordance with the Indian Pharmacopoeia. The test was performed to check any growth of micro-organism during storage or not. It included an assessment for total viable count, total fungal count, and the presence of *E. coli, Pseudomonas aeruginosa, Salmonella*, and *Staphylococcus aureus*. The test was performed on freshly prepared MDF and MDFs stored for 6 months at 25ºC and 40% relative humidity in the packaging conditions specified in stability testing. According to the Indian pharmacopoeia, the Total viable count should be less than 100 CFU per g or mL of sample, Total fungal count should be less than 10 CFU per g or mL. *E. coli, Pseudomonas aeruginosa, Salmonella*, and *Staphylococcus aureus* should be absent (Indian Pharmacopoeia 2010).

RESULTS AND DISCUSSION

For Batch F1 and F2 which is given in Table 1b, MDFs were not successfully formed, possibly due to inadequate polymer-plasticiser interaction leading to poor film integrity. Although films of Batch F3 to F6 were obtained, they adhered

Table 2a: Evaluation parameters of MDF containing Pullulan and PEG 400.

Evaluation parameters	F10	F11	F12	F13	F14	F15	F16	F17	F18
Tensile strength(kg/cm^2)	0.13±0.001	0.06±0.0009	0.11±0.001	0.13±0.001	0.09±0.0009	0.04±0.0009	0.25±0.001	0.17±0.001	0.10±0.001
% Elongation	54.54±0.8	85.9±0.2	80.05±0.2	78±0.3	79.9±0.4	87±0.17	71.26±0.33	79.51±0.17	61.53±0.59
Young's modulus(kg/cm^2)	0.06±0.001	0.007±0.00	0.021±0.0004	0.03±0.0006	0.02±0.0004	0.005±0	0.07±0.001	0.03±0.0006	0.04±0.001
Disintegration time(S)	22±1	26±0.57	33±1.52	35±1.52	35±1	38±0.577	46±1	50±0.57	24±1.15
% M.C.	9.27±0.6	8.36±0.8	8.69±1.1	8.68±0.6	9.04±0.9	9.45±0.37	7.76±0.9	5.88±0.71	9.5±0.43

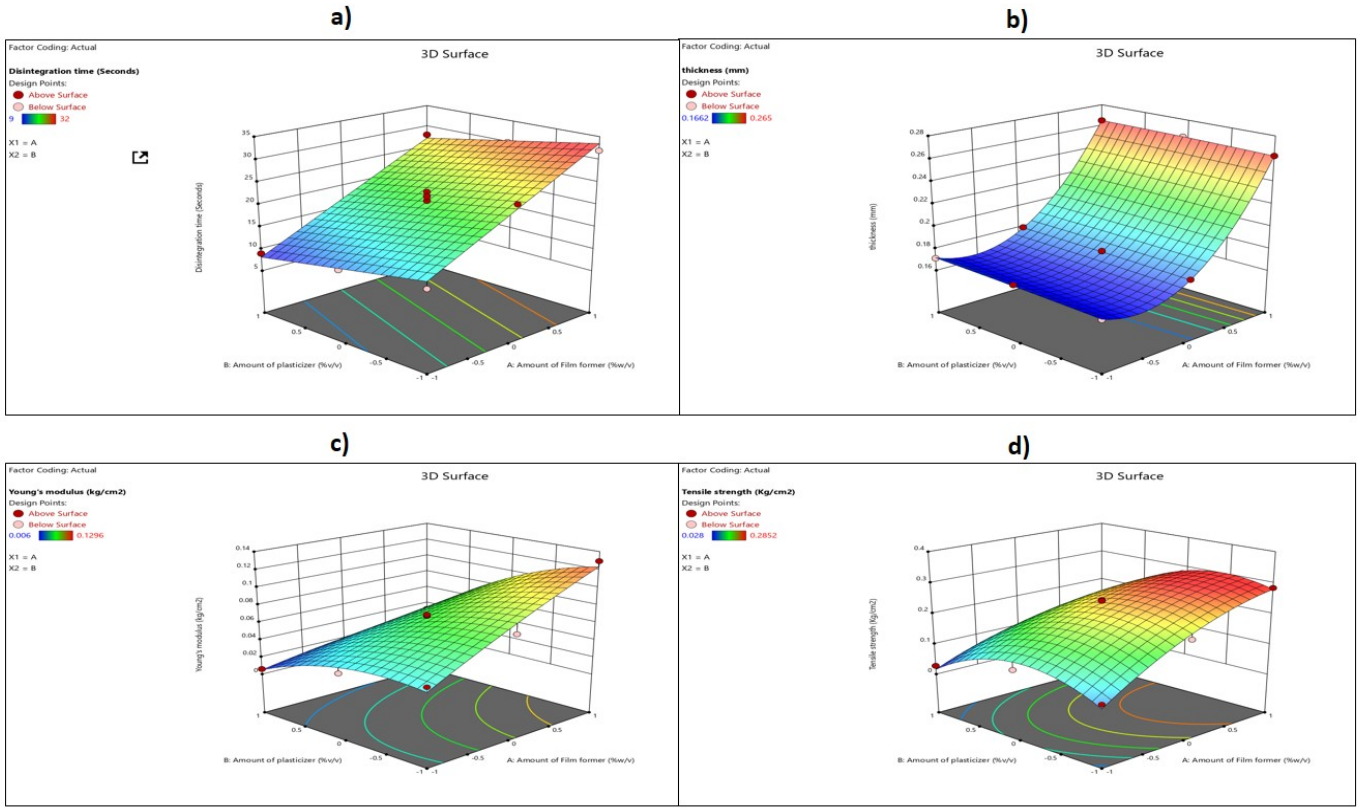

Figure 1: Surface plot for the effect of concentration of Pullulan and PEG 400 on a. Disintegration time, b. Thickness, c. Young's modulus and d. Tensile strength.

Table 2 b: Level of Pullulan as film former and PEG 400 as Plasticizer using 3^2 factorial design.

Independent Factors	Low (-1)	Medium (0)	High (+1)
Concentration of Pullulan (%w/v)	3	6	9
Concentration of PEG 400 (%w/v)	1.26	3.78	6.3

Table 2 c: General Formula of MDF for 3^2 factorial design.

Ingredients	Quantity
Ferrous Bisglycinate (%w/v)	12
Pullulan (%w/v)	-
PEG 400 (%w/v)	-
Sweet pearl P 300 DC (%w/v)	5
Tri Sodium citrate (%w/v)	1.5
Sucralose (%w/v)	0.35
Mixed fruit Flavor	q.s.
Water (mL)	100

strongly to the Petri-plates and could not be separated. In the case of Batch F7 and F8, uniform films were formed; however, the disintegration time exceeded the limit, likely due to higher polymer content or reduced porosity of the film matrix. For Batch F9, precipitation occurred after the addition of Ferrous Bisglycinate, which can be ascribed to incompatibility between the drug and the polymeric solution, or to the poor aqueous solubility.

Various batches containing Pullulan and PEG 400 were prepared as presented in Table 1c and subsequently evaluated for different parameters. As shown in Table 2 a, the tensile strength of the films ranged from 0.04 to 0.25 kg/cm², percentage elongation from 54.5 to 85.9%, Young's modulus from 0.005 to 0.07 kg/cm², disintegration time between 22 and 50 sec, and moisture content from 5.88% to 9.5%. The results indicated that Pullulan predominantly influenced the mechanical strength and disintegration behaviour of the films, whereas PEG 400 mainly affected flexibility and moisture retention.

Based on these findings, Pullulan and PEG 400 were selected as the independent variables for further optimization of the MDFs using a 3^2-factorial design, executed with Design Expert Software (Version 11). The concentration of Pullulan (X_1) and PEG 400 (X_2) served as the independent factors given in Table 2b, while disintegration time, thickness, tensile strength, and Young's modulus were considered as response variables.

The factorial design included a total of 13 experimental runs Table 2d, consisting of 9 factorial points and 4 centre points. The composition of the formulations for the central composite design is shown in Table 2c. All experimental evaluations were carried out in triplicate, and the data obtained for the 13 runs are summarized in Table 3a. Batch F22 is identified as the optimized formulation, as it met all the evaluation criteria within the limits of the target product profile, which is depicted in Table 3b.

Statistical analysis of the data using Design Expert software

Response 1: Disintegration Time

The linear regression equation for disintegration time is

$$Y = 20.85+9.5X_1-3.17X_2 \text{ ----------(4)}$$

The R^2 value for response Disintegration time is 0.96, indicating a strong fit for the model. The variation in Disintegration time ranges from 09 sec to 32 sec. Analysis of regression coefficients reveals that the concentration of pullulan positively influences, and the concentration of glycerol negatively affects the Disintegration time. Equation 4 states pullulan has a greater influence on disintegration time compared to glycerol as it has a greater regression coefficient.

Response 2: Thickness

The polynomial equation for Thickness is

$$Y = 0.1771+0.0473X_1+ 0.0018X_2 -0.007X_1X_2+0.0399X_1^2- 0.0004X_2^2\text{----------(5)}$$

The R^2 value for response Thickness is 0.9995, indicating a strong fit for model. The variation in thickness ranges from 0.175 to 0.265mm. From the regression coefficient, it was concluded that the thickness of the mouth-dissolving film is more positively influenced by the concentration of Pullulan as compared to the concentration of Glycerol. This indicates that increasing the amount of Pullulan in the formulation has a greater impact on enhancing the film's thickness, which is an important factor for achieving the desired physical characteristics of the final product.

Response 3 Young's modulus

The polynomial equation for Young's modulus is,

$$Y = 0.0659+0.0283X_1-0.03X_2-0.0156X_1X_2-0.0033X_1^2-0.0141X_2^2 \text{ ---------- (6)}$$

The R^2 value for Young's modulus is 0.9706, indicating a strong model fit. The variation in Young's modulus response from all 13 batches was from 0.0016 to 0.1296 Kg/cm². From the regression coefficient, it was concluded that Young's modulus is positively affected by the concentration of Pullulan and negatively affected by the concentration of PEG 400.

Response 4 Tensile strength

The polynomial equation for Tensile strength is,

$$Y = 0.2381+0.0847X_1-0.047X_2-0.0298X_1X_2-0.03715X_1^2-0.0821X_2^2 \text{---------- (7)}$$

The R^2 value for Tensile strength is 0.9812, indicating the strong model fit. The variation in Tensile strength response from all 13 batches was from 0.065-0.285 Kg/cm^2. From the regression coefficient, it was concluded that Young's modulus is positively affected by the concentration of Pullulan and negatively affected by the concentration of PEG 400.

According to Table 3c, it can be inferred that the concentration of Pullulan and the concentration of PEG 400 exert a statistically significant influence on the evaluated responses - disintegration time, thickness, Young's modulus, and tensile strength - as evidenced by their p-values being less than 0.05. Furthermore, a quadratic effect of concentration of Pullulan was observed on thickness and tensile strength**,** while the quadratic effect of concentration of PEG 400 was noted on Young's modulus and tensile strength. In addition, a significant interaction effect between Pullulan and PEG 400 concentrations was identified for Young's modulus and tensile strength, indicating synergistic influences of these formulation variables on the mechanical properties of the films.

The 3D surface and contour plots generated using the software for Disintegration time, Thickness, Young's modulus and Tensile strength are presented in Figures 1 and 2 respectively.

F22 batch was further considered for the pH optimization and flavor selection. To optimize the pH of the film formulation, varying concentrations of tri-sodium citrate (1.5, 2.0, 2.5, 3.0, and 3.5% w/v) were evaluated. The formulation containing 3.5% w/v tri-sodium citrate exhibited a pH of 5.29±0.01, which lies within the desired pH range of 5-7. Therefore, 3.5% w/v trisodium citrate was selected as the optimal concentration for pH adjustment in the final formulation.

Three flavoring agents-mixed fruit, coffee, and strawberry-were evaluated for taste masking and overall palatability through sensory assessment involving six human volunteers. Among the tested options, the strawberry flavor was preferred by all participants, indicating superior acceptability in terms of taste, aroma, and aftertaste.

Dissolution studies were conducted for the optimized batch (F22). From Figure 3a it was concluded that within 15 min, more than 85% of Ferrous Bisglycinate has been dissolved.

The formulated film exhibited physical instability when stored at 45°C and 75% RH, becoming soft and sticky after one month. In contrast, the film remained physically stable under storage conditions of 25°C and 40% RH for a period of six months. The corresponding results are presented in Table 4a. As shown in Figure 3b, the cumulative percentage drug release profile demonstrated no significant variation throughout the six-month stability study. According to Table 4a**,** the calculated f_1 values for all batches were below 50, while the f_2 values ranged between 50 and 100, indicating similarity in dissolution profiles. Furthermore, no significant changes were observed in mechanical strength, moisture content, or disintegration time during the study period.

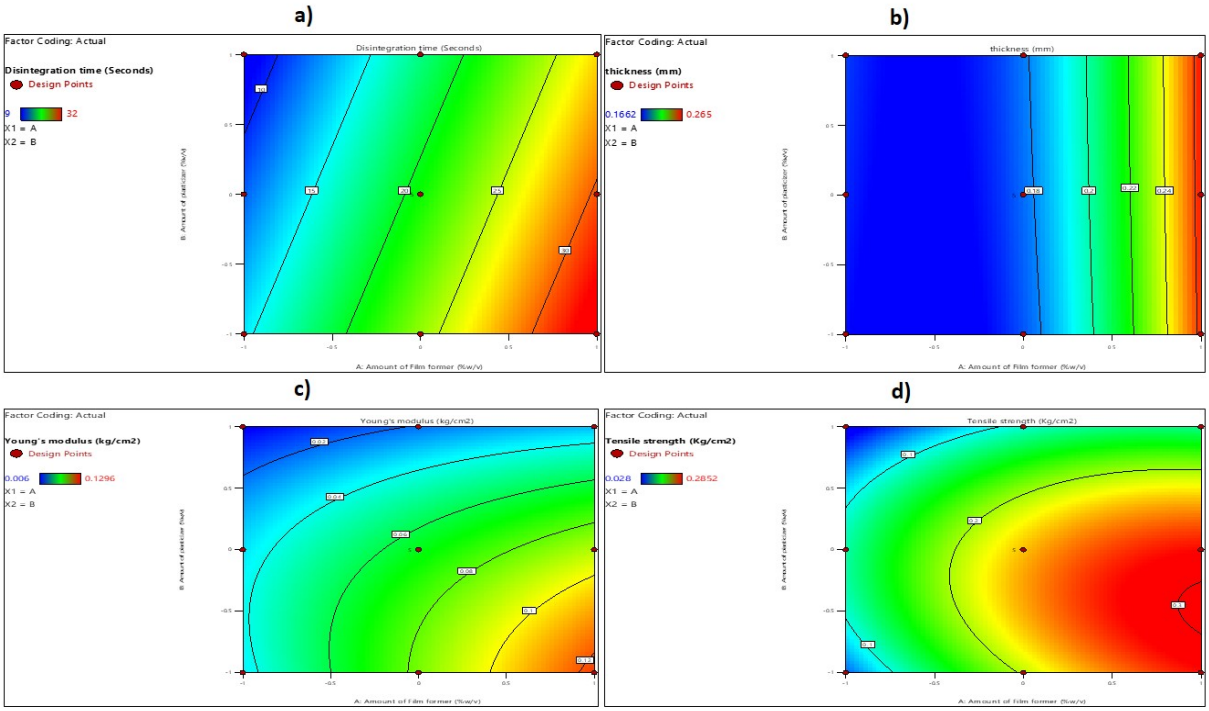

Figure 2: Contour Plot for the effect of concentration of Pullulan and PEG 400 on a. Disintegration time, b. Thickness, c. Young's modulus and d. Tensile strength.

Table 2 d: 13 Runs of 3^2 factorial design 9 factorial runs and 4 center points.

Runs	Batch No.	Coded value of Pullulan	Coded value of PEG 400	Concentration of Pullulan (%w/v)	Concentration of PEG 400(%w/v)	Temperature of solution (°C)	Brix Value (%) measured at 30°C
1	F19	0	0	6	3.78	28.6	22.2
2	F20	0	-1	6	1.26	28.6	19.4
3	F21	0	0	6	3.78	28.6	22.2
4	F22	0	0	6	3.78	28.6	22.2
5	F23	-1	-1	3	1.26	28.6	18
6	F24	1	0	9	3.78	28.8	23.4
7	F25	0	0	6	3.78	28.6	22.2
8	F26	1	1	9	6.3	28.6	23
9	F27	0	0	6	3.78	28.6	22.2
10	F28	-1	0	3	3.78	28.8	18.4
11	F29	0	1	6	6.3	28.6	22.8
12	F30	-1	1	3	6.3	28.6	20.8
13	F31	1	-1	9	1.26	28.8	22

Table 3a: Evaluation of MDF of 3^2 factorial design

Batch No.	D.T (Sec)	Thickness (mm)	Tensile strength (kg/cm²)	Young's Modulus (Kg/cm²)	% elongation	% M.C.	% assay
F19	23±1	0.18±0.002	0.24±0.003	0.07±0.001	71.59±0.32	6.46±0.51	103.66±0.54
F20	25±1	0.18±0.003	0.19±0.002	0.07±0.001	61.53±0.59	4.96±0.65	103.12±0.62
F21	21±1	0.18±0.002	0.24±0.002	0.07±0.0008	71.80±0.49	6.77±0.81	101.80±0.47
F22	21±0.58	0.18±0.002	0.25±0.002	0.07±0.0007	71.62±0.28	5.33±0.47	101.7±0.74
F23	13±1	0.18±0.003	0.07±0.003	0.04±0.0009	37.47±1.60	3.57±0.02	102.05±0.92
F24	30±0.58	0.26±0.002	0.28±0.001	0.082±0.001	70.24±0.35	6.03±0.6	99.65±0.71
F25	22±0.58	0.18±0.003	0.24±0.003	0.07±0.0004	71.48±0.50	6.47±0.43	103.90±0.54
F26	28±0.58	0.27±0.002	0.13±0.004	0.03±0.0015	74.91±0.39	3.65±0.02	104.40±0.54
F27	22±1	0.18±0.001	0.25±0.005	0.07±0.001	71.80±0.49	6.03±0.83	101.51±1.34
F28	11±1	0.18±0.003	0.09±0.001	0.03±0.0002	69.13±0.38	5.63±0.08	99.71±0.54
F29	14±0.58	0.18±0.002	0.09±0.003	0.018±0.0009	80.72±0.23	6.81±0.52	102.45±0.38
F30	9±0.58	0.19±0.003	0.03±0.003	0.001±0.0007	77.20±0.32	5.52±0.03	98.58±2.11
F31	32±1	0.26±0.002	0.29±0.004	0.13±0.0003	54.54±0.83	6.78±0.64	99.23±1.08

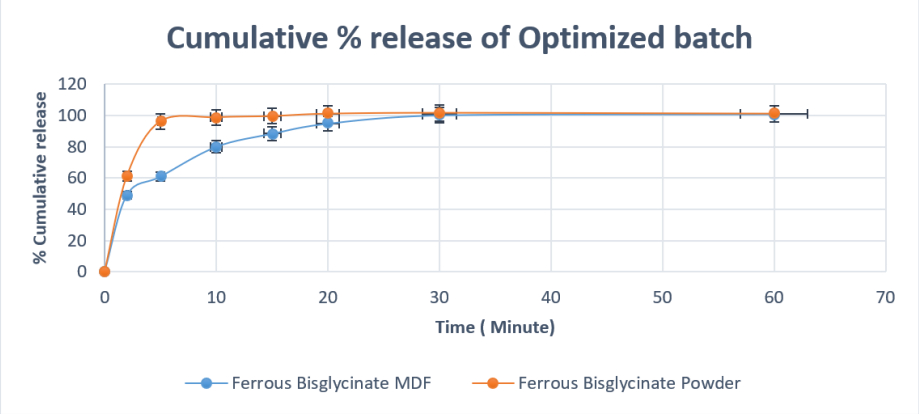

Figure 3a: Dissolution studies of Optimized batch and pure Ferrous Bisglycinate powder (F22).

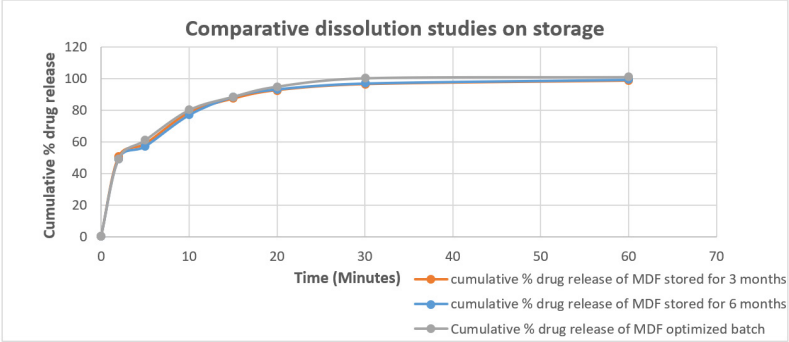

Figure 3b: Dissolution studies of Optimized batch, MDF stored for 6 months and pure Ferrous Bisglycinate powder (F22).

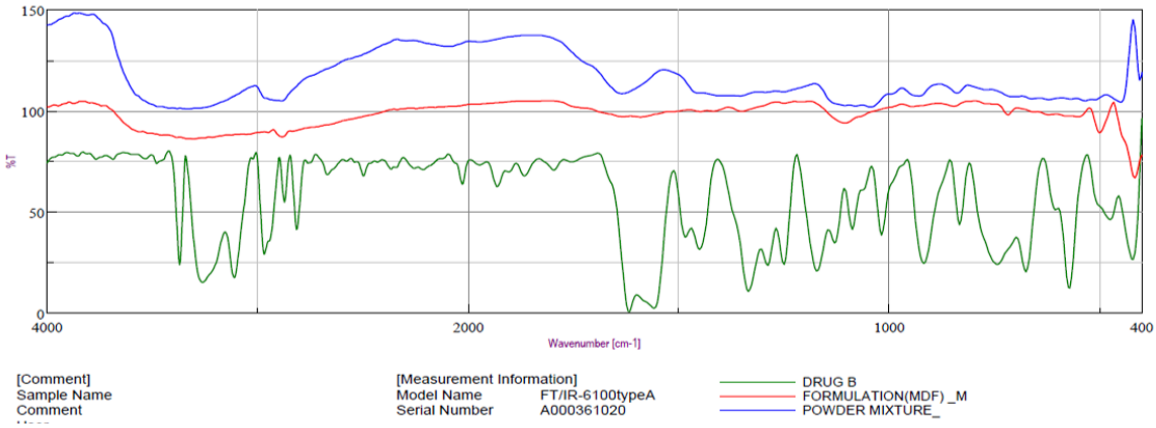

Figure 3c: Comparison of FTIR Spectra of pure Ferrous Bisglycinate powder (Drug B), freshly prepared drug excipient powder mixture and MDF of optimized batch (F22).

Therefore, it can be inferred that the optimized film formulation remained stable under storage conditions (25°C/40% RH) for a duration of six months.

From Figure 3c FTIR spectra reveal that no new peaks or significant shifts are visible. So, no major chemical interaction or degradation is indicated after formulation into mouth mouth-dissolving film.

The taste evaluation behaviour of optimized MDF of Ferrous Bisglycinate using an e-tongue shows that the First Principal Component (PC1) accounts for 86.092% of the variance, while the Second Principal Component (PC2) explained 12.7% of the variance which is demonstrated in Figure 4a. Together, these two components represented 98.81% of the total data variability, which demonstrates that the model accurately reflects the true characteristics of the samples and provides a robust basis for interpretation. The replicate points of pure Ferrous Bisglycinate are tightly grouped on the right side of the PCA plot, whereas those of MDF clustered closely on the left side, confirming minimal intra-sample variability. The discrimination index is 99 further validated the clear separation between the two clusters, highlighting their distinct taste profiles. As summarized in Table

4c, MDF exhibited comparatively higher responses in PKS, NMS sensor indicates the enhanced Umami, which is good for taste masking and palatability. MDF exhibited AHS response decrease which suggests a reduction in sourness. MDF has more response in CPS and SCS, indicating the increased saltiness. The taste fingerprint (Figure 4b) confirmed the divergence between the two samples, emphasizing the different sensory signatures. Bitterness quantification was carried out using the Astree electronic tongue, with quinine sulphate serving as the reference standard. The calibration showed excellent reliability, with a correlation coefficient of R^2=0.9626, confirming strong linearity. Comparative evaluation revealed that MDF exhibited a less bitter profile than Ferrous Bisgycinate, with fewer responses across multiple sensors. This result demonstrated the effectiveness of taste screening using e-tongue analysis, as it confirmed the distinct taste profile of MDF from pure Ferrous Bisglycinate powder.

The taste evaluation of the optimized formulation (0 month) and its stability batches (stored for 3, 6 months) was carried out using six healthy human volunteers. The average taste scores assigned by six volunteers are presented in Table 4b. The

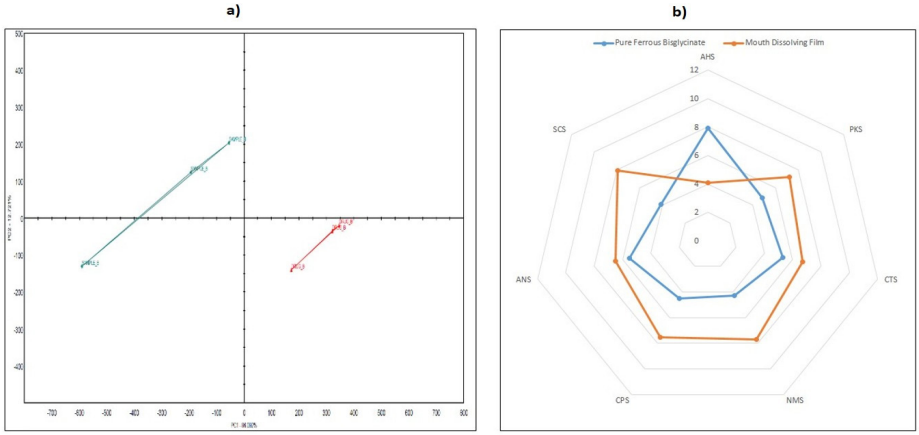

Figure 4: a. Principle component analysis, b. e-tongue taste screening of drug B (Pure Ferrous Bisglycinate and sample B (MDF).

Table 3 b: Target product profile of MDF.

Evaluation parameters	Target
Thickness (mm±S.D)	0.15-0.3
Tensile strength (kg/cm^2±S.D)	0.2-0.3
% Elongation (%±S. D)	50-80
Young's modulus(kg/cm^2±S.D)	0.05-0.15
Disintegration time (sec ±S. D)	5-30
% Moisture content (%±S. D)	4-7
% assay (%±S. D)	95-110
pH (±S. D)	5-7

Table 3 c: *p* values for the responses given design expert softwares for the factorial run *(F19-F31).*

Response	*p* value				
	A	B	AB	A^2	B^2
Disintegration time	<0.0001	0.0009	-	-	-
Thickness	<0.0001	0.0052	0.2530	<0.0001	0.5380
Young's modulus	<0.0001	<0.0001	0.0037	0.477	0.0147
Tensile Strength	<0.0001	<0.0002	0.0075	<0.0061	<0.0001

A: Regression coefficient for Concentration of Pullulan.
B: Regression coefficient for Concentration of PEG 400.
AB: Regression coefficient for the interaction term.
A^2: Regression coefficient for the quadratic term of Pullulan.
B^2: Regression coefficient for the quadratic term of PEG 400.

Table 4a: Evaluation parameters of optimized MDF (Batch F22) subjected to stability studies(25°C / 40% RH).

No of months	% drug release in 30 min	F1	F2	Tensile strength (kg/cm²±S.D)	Young's Modulus (kg/cm²±S.D)	D.T. (Sec)	% Elongation	% M.C.
0	100.31	-	-	0.245±0.002	0.069±0.0007	21±0.58	71.62±0.28	5.33±0.47
3	96.63	3.06	77.84	0.22±0.007	0.066±0.002	22.6±1.52	70.70±0.5	5.81±0.80
6	97.15	2.88	76.61	0.195±0.005	0.058±0.002	23.6±0.57	70±0.42	6.55±0.76

Table 4b: Taste Evaluation of MDF Using Human Volunteers at 0, 3, and 6 Months of Storage at 25 °C / 40% RH.

Taste Evaluation	Observed average score (0 months)	Conclusion	Observed average score (3 months)	Conclusion	Observed average score (6 months)	Conclusion
Metallic taste	3.33±0.5	Acceptable	3.16±0.4	Acceptable	3.16±0.4	Near to Acceptable
Sweetness	2.33±0.51	Slightly sweet	2.66±0.51	Acceptable	2.5±0.54	Acceptable
Mouth feel	5±0	Smooth	5±0	Smooth	5±0	Smooth
Flavor	3.66±0.51	Pleasant	3.66±0.51	Pleasant	3.66±0.51	Pleasant
Overall palatability	4±0	Good	4±0	Good	4±0	Good
Bitter after taste	3.5±0.54	Acceptable to slightly bitter	3.66±0.51	Slightly bitter	3.66±0.51	Slightly bitter
In vivo D.T. (Sec)	10.33±0.51	<30	9.8±0.98	<30	9.5±0.83	<30

Table 4c: Taste screening data of Pure Ferrous Bisglycinate and MDF for seven sensors.

Sensor	Pure Ferrous Bisglycinate	Mouth Dissolving Film
AHS	7.90	4.10
PKS	4.80	7.20
CTS	5.30	6.70
NMS	4.30	7.70
CPS	4.50	7.50
ANS	5.50	6.50
SCS	4.10	7.90

finding indicated that the developed MDF exhibited satisfactory palatability with disintegration time approximately 9-10 sec. The slight in disintegration time was attributed to the mechanical pressure exerted by the tongue against the palate during *in vivo* administration.

The obtained data were subjected to statistical analysis using one-way Analysis of Variance (ANOVA) in Microsoft Excel to determine any significant variation in average taste scores over three different storage intervals (0, 3, and 6 months). The *p*-values were found to be greater than 0.05, which is above the predefined level of significance. Therefore, it was inferred that no statistically significant difference existed in the taste evaluation scores over the 6-month storage period, confirming the palatability stability of the formulation.

The results of the microbial contamination test for MDF (F22 batch) were found to comply with the Indian Pharmacopeia. The total viable count was less than 10 CFU/gm, and the total fungal count was less than 10 CFU/gm. Additionally, *E. coli, Pseudomonas aeruginosa, Salmonella,* and *Staphylococcus aureus* were found absent in both freshly prepared and stored for 6 months.

The proposed MDF formulation demonstrates strong potential for successful scale-up from small-scale petri-plate casting to a continuous solvent-casting process. Pullulan, a film-forming polysaccharide, provides excellent wet-film strength and yields flexible, cohesive films upon plasticization (Prajapati *et al*., 2018). Polyethylene Glycol 400 (PEG 400), a widely utilized hydrophilic plasticizer, effectively reduces the polymer's glass transition temperature and enhances mechanical resilience (Alayoubi *et al*., 2017). Sweet Pearl P300DC functions as a bulking agent and humectant, contributing to improved palatability while minimizing the risk of crystallization under appropriate formulation conditions (Sheet, 2019).

The physicochemical compatibility of these excipients enables the development of uniform, mechanically stable MDFs suitable for aqueous solvent-casting operations. Moreover, their properties support process scalability through continuous coating, controlled drying, and efficient handling. Optimal performance can be achieved by fine-tuning of critical process parameters, including homogeneity of API dispersion, casting solution viscosity, wet film thickness, drying temperature, residence time on the casting surface, and residual moisture content (Özcan Bülbül *et al*., 2019).

CONCLUSION

This study reports the successful formulation and optimization of a MDF containing Ferrous Bisglycinate, with a particular emphasis on the selection and performance of film-forming and plasticizing agents. Pullulan was employed as the primary film-former owing to its excellent film-forming properties, While PEG 400 was incorporated as a plasticizer to enhance flexibility and mechanical properties. The optimized formulation exhibited desirable characteristics, including mechanical properties, rapid disintegration, satisfactory dissolution behaviour, appropriate moisture content, stability under controlled conditions, acceptable microbial quality and favourable *in vivo* taste evaluation outcomes.

The MDF demonstrated a notably improved organoleptic profile compared to pure Ferrous Bisglycinate powder, characterized by a reduction in bitterness and enhanced overall palatability. These findings indicate that the developed MDF may offer a more patient-friendly dosage form, particularly suitable for paediatric populations, thereby contributing to improved adherence in iron supplementation therapies.

While the formulation remained stable throughout the evaluation period, its hygroscopic nature necessitates the implementation of appropriate packaging and storage strategies to preserve product integrity. Further work may include extended long-term stability assessments and structured taste evaluation studies involving trained paediatric participants with adequate cognitive abilities. This novel MDF platform holds significant promise as an innovative, patient-centric approach for combating iron deficiency and associated malnutrition.

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ABBREVIATIONS

MDF: Mouth Dissolving Film; **HPMC:** Hydroxy Propyl Methyl cellulose; **PEG:** Poly ethylene Glycol; **DT:** Disintegration Time; **FTIR:** Fourier Transform Infrared; **IDA:** Iron Deficiency Anaemia, **WHO:** World Health Organization; **FSSAI:** Food Safety Standard Authority of India; **%W/V:** percentage weight by volume; **mL:** Millilitres; **Q.S.:** Quantity Sufficient; **Kg/Cm²:** Kilogram per centimetre square; **mm:** Millimetres; **SD:** Standard Deviation; **RH:** Relative Humidity; **PCA:** Principal component analysis; **CFU:** Colony Forming Units; ANOVA**:** Analysis of Variance.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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AUTHOR CONTRIBUTION

Conceptualization and design of the experiment: all authors.

Methodology and analysis: Ms. Jahanvi Patel.

Project administration: all authors.

Supervision: Dr. Tejal Mehta.

Writing original draft: Ms. Jahanvi Patel.

Writing, reviewing and editing: all authors.

REFERENCES

Ahmed, T., Hossain, M., and Sanin, K. I. (2012). Global burden of maternal and child undernutrition and micronutrient deficiencies. *Annals of Nutrition and Metabolism*, *61*(suppl 1), 8-17. https://doi.org/10.1159/000345165

Alayoubi, A., Haynes, L., Patil, H., Daihom, B., Helms, R., and Almoazen, H. (2017). Development of a fast dissolving film of epinephrine hydrochloride as a potential anaphylactic treatment for pediatrics. *Pharmaceutical Development and Technology*, *22*(8), 1012-1016. https://doi.org/10.3109/10837450.2015.1131715

Authority, P. B. Y., and Delhi, N. E. W. (2018). *Supplements, Nutraceuticals, Food for Special Dietary Use, Food for Special Medical Purpose, Functional Food and Novel Food) Regulations, 2016*. *2016*(D).

BRISE, H., and HALLBERG, L. (1962). Absorbability of Different Iron Compounds. *Acta Medica Scandinavica*, *171*(suppl 376), 23-37. https://doi.org/10.1111/j.0954-6820.1962.tb18680.x

Chan, L. N., and Mike, L. A. (2014). The science and practice of micronutrient supplementations in nutritional anemia: An evidence-based review. *Journal of Parenteral and Enteral Nutrition*, *38*(6), 656-672. https://doi.org/10.1177/0148607114533726

Degrees Brix to Specific Gravity Conversion Tables (2011). *January*, 1-8.

Diaz, D. A., Colgan, S. T., Langer, C. S., Bandi, N. T., Likar, M. D., and Van Alstine, L. (2016). Dissolution Similarity Requirements: How Similar or Dissimilar Are the Global Regulatory Expectations? *AAPS Journal*, *18*(1), 15-22. https://doi.org/10.1208/s12248-015-9830-9

Dixit, R. P., and Puthli, S. P. (2009). Oral strip technology: Overview and future potential. *Journal of Controlled Release*, *139*(2), 94-107. https://doi.org/10.1016/j.jconrel.2009.06.014

Gupta, H., Sharma, A., Kumar, S., and Roy, S. (2009). E-Tongue: A Tool for Taste Evaluation. *Recent Patents on Drug Delivery and Formulation*, *4*(1), 82-89. https://doi.org/10.2174/187221110789957309

ICH. (2003). International Conference on Harmonization (ICH). Guidance for industry: Q1A(R2) Stability Testing of New drug Substances and Products. *ICH Harmonised Tripartite Guideline*, *4*(1-24).

Indian Pharmacopoeia 2010. (2010). No Title. *Indian Pharmacopoeia Commission, Gaziabad*, *I*, 677.

Jain, P., Gupta, A., and Darwhekar, G. (2023). An Detailed Overview on Mouth Dissolving Film. *Journal of Drug Delivery and Therapeutics*, *13*(7), 172-176. https://doi.org/10.22270/jddt.v13i7.6121

John Anthony Considine, E. J. F. (2023). *Essential analyses,A Complete Guide to Quality in Small-Scale Wine Making* (2023 (Ed.); second, p. Pages 163-180). Academic Press. https://doi.org/ISBN 9780323992879,https://doi.org/10.1016/B978-0-323-99287-9.00003-6.

Joshi, P., Patel, H., Patel, V., and Panchal, R. (2012). Formulation development and evaluation of mouth dissolving film of domperidone. *Journal of Pharmacy and Bioallied Sciences*, *4*(SUPPL 1), 108-109. https://doi.org/10.4103/0975-7406.94159

Karki, S., Kim, H., Na, S. J., Shin, D., Jo, K., and Lee, J. (2016). Thin films as an emerging platform for drug delivery. *Asian Journal of Pharmaceutical Sciences*, *11*(5), 559-574. https://doi.org/10.1016/j.ajps.2016.05.004

Kumar, D., Singh, A., and Jayasundar, R. (2021). Challenges in using Electronic tongue to study rasa of plants: II. Impact of solvent and concentration on sensor response and taste ranking. *Journal of Ayurveda and Integrative Medicine*, *12*(2), 238-244. https://doi.org/10.1016/j.jaim.2020.12.010

Lambros, M., Tran, T. H., Fei, Q., and Nicolaou, M. (2022). Citric Acid : A Multifunctional Pharmaceutical Excipient The salt and The form of trisodium citrate is por [11]. Detailed analyses of the structural, spectral, and thermal p such as citrates, succinates, and alpha-ketoglutarate, is transporte. *Pharmaceutics*, *14(5)*, *972*.

Mathur, R., and Swaminathan, S. (2018). National Ethical Guidelines for Biomedical and Health Research Involving Human Participants, 2017: A commentary. In *Indian journal of medical ethics* 148(3), 279. https://doi.org/10.20529/IJME.2018.065

MD, S., KUMAR, S., and DODDAYYA, H. (2023). Fabrication and Evaluation of Mouth-Dissolving Films of Domperidone. *International Journal of Current Pharmaceutical Research*, *15*(2), 36-43. https://doi.org/10.22159/ijcpr.2023v15i2.2088

Mishra, R., and Amin, A. (2011). Formulation and characterization of rapidly dissolving films of cetirizine hydrochloride using pullulan as a film forming agent. *Indian Journal of Pharmaceutical Education and Research*, *45*(1), 71-77.

Nam, S. H., Lee, J., Kim, E., Koo, J. W., Shin, Y., and Hwang, T. M. (2023). Electronic tongue for the simple and rapid determination of taste and odor compounds in water. *Chemosphere*, *338*(June), 139511. https://doi.org/10.1016/j.chemosphere.2023.139511

Özcan Bülbül, E., Mesut, B., Cevher, E., Öztaş, E., and Özsoy, Y. (2019). Product transfer from lab-scale to pilot-scale of quetiapine fumarate orodispersible films using quality by design approach. *Journal of Drug Delivery Science and Technology*, *54*, 101358. https://doi.org/10.1016/j.jddst.2019.101358

Pacheco, M. S., Barbieri, D., da Silva, C. F., and de Moraes, M. A. (2021). A review on orally disintegrating films (ODFs) made from natural polymers such as pullulan, maltodextrin, starch, and others. *International Journal of Biological Macromolecules*, *178*, 504-513. https://doi.org/10.1016/j.ijbiomac.2021.02.180

Palezi, S. C., Fernandes, S. S., and Martins, V. G. (2023). Oral disintegration films: applications and production methods. *Journal of Food Science and Technology*, *60*(10), 2539-2548. https://doi.org/10.1007/s13197-022-05589-9

Pantopoulos, K. (2024). Oral iron supplementation: New formulations, old questions. *Haematologica*, *September*, 109(9) 2790-2801. https://doi.org/10.3324/haematol.2024.284967

Prajapati, V. D., Chaudhari, A. M., Gandhi, A. K., and Maheriya, P. (2018). Pullulan based oral thin film formulation of zolmitriptan: Development and optimization using factorial design. *International Journal of Biological Macromolecules*, *107*, 2075-2085. https://doi.org/10.1016/j.ijbiomac.2017.10.082

Reuther, M., Rollet, N., Debeaufort, F., and Chambin, O. (2025). Orodispersible films prepared by hot-melt extrusion versus solvent casting. *International Journal of Pharmaceutics*, *675*(January). https://doi.org/10.1016/j.ijpharm.2025.125536

Salawi, A. (2022). An Insight into Preparatory Methods and Characterization of Orodispersible Film-A Review. *Pharmaceuticals*, *15*(7). https://doi.org/10.3390/ph15070844

Santiago, P. (2012). Ferrous versus ferric oral iron formulations for the treatment of iron deficiency: A clinical overview. *The Scientific World Journal*, *2012*. https://doi.org/10.1100/2012/846824

Senthilkumar, K., and Vijaya, C. (2015). Formulation Development of Mouth Dissolving Film of Etoricoxib for Pain Management. *Advances in Pharmaceutics*, *2015*, 1-11. https://doi.org/10.1155/2015/702963

Sheet, S. D. (2019). *SAFETY DATA SHEET SWEETPEARL ® P300 DC SECTION 4 : First aid measures*. 1-7.

Sunita, A. C., Ankit, B. C., and Tejal, A. M. (2012). Formulation development and optimization of polyox based quick dissolving film of quetiapine. *Journal of Pharmacy and Bioallied Sciences*, *4*(SUPPL.), 19-20. https://doi.org/10.4103/0975-7406.94123

Uses, F. (2003). *FERROUS GLYCINATE (processed with CITRIC ACID) FUNCTIONAL USES*. *4*, 0-2.

Wang, Z., Li, J., Hong, X., Han, X., Liu, B., Li, X., Zhang, H., Gao, J., Liu, N., Gao, X., and Zheng, A. (2021). Taste Masking Study Based on an Electronic Tongue: the Formulation Design of 3D Printed Levetiracetam Instant-Dissolving Tablets. *Pharmaceutical Research*, *38*(5), 831-842. https://doi.org/10.1007/s11095-021-03041-9

World Health Organization. Anaemia. WHO Health Topics. Available from: https://www.who.int/health-topics/anaemia#tab=tab_1 *[Accessed 24 June 2025]*. (n.d.).

World Health Organization. Malnutrition. WHO Health Topics. Available from: https://www.who.int/health-topics/malnutrition#tab=tab_1 *[Accessed 24 June 2025].No Title*. (n.d.).

World Health Organization. (2016). Guideline Daily Iron. *Daily Iron Supplimentation in Infants and Children*, 44.

Yu, X., Chen, L., Ding, H., Zhao, Y., and Feng, J. (2019). Iron transport from ferrous bisglycinate and ferrous sulfate in DMT1-knockout human intestinal caco-2 cells. *Nutrients*, *11*(3), 1-14. https://doi.org/10.3390/nu11030485

Yunarti, R. T., Zulys, A., Harahap, L. Y., Saroh, M., and Pramukti, A. (2018). Effectiveness of Iron Fortification on Soy-Based Foods Using Ferrous Bisglycinate in the Presence of Phytic Acid. *Makara Journal of Science*, *17*(1), 11-16.

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